The prognostic role of a gene signature from tumorigenic breast-cancer cells.

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Public Summary:

Scientific Abstract:
BACKGROUND: Breast cancers contain a minority population of cancer cells characterized by CD44 expression but low or undetectable levels of CD24 (CD44+CD24-/low) that have higher tumorigenic capacity than other subtypes of cancer cells. METHODS: We compared the gene-expression profile of CD44+CD24-/low tumorigenic breast-cancer cells with that of normal breast epithelium. Differentially expressed genes were used to generate a 186-gene "invasiveness" gene signature (IGS), which was evaluated for its association with overall survival and metastasis-free survival in patients with breast cancer or other types of cancer. RESULTS: There was a significant association between the IGS and both overall and metastasis-free survival (P<0.001, for both) in patients with breast cancer, which was independent of established clinical and pathological variables. When combined with the prognostic criteria of the National Institutes of Health, the IGS was used to stratify patients with high-risk early breast cancer into prognostic categories (good or poor); among patients with a good prognosis, the 10-year rate of metastasis-free survival was 81%, and among those with a poor prognosis, it was 57%. The IGS was also associated with the prognosis in medulloblastoma (P=0.004), lung cancer (P=0.03), and prostate cancer (P=0.01). The prognostic power of the IGS was increased when combined with the wound-response (WR) signature. CONCLUSIONS: The IGS is strongly associated with metastasis-free survival and overall survival for four different types of tumors. This genetic signature of tumorigenic breast-cancer cells was even more strongly associated with clinical outcomes when combined with the WR signature in breast cancer.